Remarks

Claims 1-23 and 26 are under consideration. These claims define a method of treating advanced prostate cancer by the administration of an androgen suppressing amount of a LHRH agonist analog together with calcitriol in an amount sufficient to enhance the effectiveness of the LHRH agonist analog.

The continued rejection of claims 1-4 and 16-23 under 35 U.S.C. 103(a) as unpatentable over Garnick et al. in view of Beer et al. and further in view of Lu et al. is not warranted, and is hereby traversed.

As recognized by the Examiner, neither Garnick et al. nor Lu et al. teach the administration of leuprolide together with calcitriol. Neither does Beer et al.

This secondary reference only describes the co-administration of calcitriol and docetaxel, paclitaxel and platinum compounds. Beer et al. contains no suggestion whatsoever that leuprolide, an LHRH agonist, or any other LHRH agonist analog should or could be substituted for docetaxel, paclitaxel or platinum compound. There must be some teaching in the prior art that supports the combination. DCS Hosp. Sys., Inc. V. Montefiore Hosp., 4732 F.2d 1572, 1577; 221 U.S.P.Q. 929, 933 (Fed. Cir. 1984). Here there is none. Additionally, no predictability has been shown as to the effect of calcitriol when combined with an LHRH-R agonist.

The teachings of Garnick et al. Have been mischaracterized as well. To treat prostate cancer, Garnick et al. teaches the administration of LHRH-R antagonist prior to surgery. Leuprolide is not a LHRH-R antagonist, rather a LHRH-R agonist which is administered only after the treatment with a LHR-R antagonist (Garnick et al., Examples 2 and 3). Nothing in Garnick et al. would have led one of ordinary skill, whatever that skill level may have been, to (1) ignore the express teachings of Garnick et al. vis-a-vis the use of LHRH-R antagonist and instead (2) administer calcitriol together with leuprolide, a LHRH-R agonist. Also, nothing in Garnick et al. would have led one of ordinary skill to the Beer et al. reference. Furthermore, it is well established that the asserted interpretation of prior art cannot be inoperable. In re Gordon, 733 F.2d 900, 902; 221 U.S.P.Q. 1175, (Fed. Cir. 1984).

The conclusion is inescapable that the attempted combination of Garnick et al. and Beer et al. has been arrived at only by an impermissible hindsight reconstruction of the claimed invention using applicant's own teachings as a guide. One of ordinary skill would not have attempted the combination of these particular references based on the teachings thereof. There are no teachings in Garnick et al. that would have led on of ordinary skill to Beer et al. Likewise, there are no teachings in Beer et al. that would have led one of ordinary skill to Garnick et al.

The Examiner's contention that the present claims do not exclude the use of LHRH-R antagonists is not well taken. One of ordinary skill, whatever that skill level may be, would not have had any reason whatsoever to co-administer an agonist together with an antagonist. No rationale has been advanced by the Examiner why one of ordinary skill would have done so. Besides, one cannot use hindsight reconstruction to pick and choose among isolated prior art disclosures to vitiate the claimed invention. In re Fine, 837 F.2d 1071, 1075, 5 U.S.P.Q. 2d 1596, 1600 (Fed. Cir. 1988).

Lu et al. does not cure the defects of Garnick et al. or Beer et al. as references against the present claims. The amino acid residue sequence of Leuprolide is not an issue here. The Examiner agrees.

Further, as also recognized by the Examiner, the express limitations of claims 17, 19, 21, 22 and 23 are not taught by Garnick et al.

The level of ordinary skill in the pertinent art has not been resolved in this case, thus on the present record it cannot be determined what limitations would or would not have been obvious to one of ordinary skill. A mere statement by the Examiner that the level of ordinary skill is set forth by the references provided is of no moment, and does not support the findings of fact mandated by Graham v. John Deere, 383 U.S. 1, 17, 148 U.S.P.Q. 459 (1966). The onus is on the Examiner to make out a *prima facie* case of obviousness for the claimed invention. The Examiner has failed to do so. The rejection based on 35 U.S.C. 103(a) is not supportable, and should be withdrawn.

The continued rejection of claims 1, 5-15 and 26 under 35 U.S.C. 103(a) as unpatentable over Garnick et al. in view of Beer et al., Conway et al. and Chen likewise is unwarranted, and is traversed as well.

Garnick et al. and Beer et al. fail as references against claims 1, 5-15 and 26 for the same reasons as those advanced hereinabove. Additionally, as recognized by the Examiner, the express limitation of 1 to about 30 micrograms of calcitriol with a polysorbitan as called for in claims 6, 7, 12 and 26 also is not taught. Likewise, the express limitation of 5 to about 30 micrograms of calcitriol with a polysorbitan as called for in claims 12 and 13 is not taught.

The Examiner's assertion that "obvious to try" is an appropriate test of obviousness in this case is not supported by the record. The contention that "...there were limited number of methodologies available to do so, such as those of Beer et al. and Garnick et al., is not supported by the record. The examiner has adduced no evidence that the Garnick et al. and Beer et al. methodologies indeed were the only methodologies available to one of ordinary skill in the art. Beer et al. discuss the treatment of androgen - independent prostate cancer using calcitriol to enhance the activity of docetaxel, paclitaxel, and platinum compounds, not the LHRH-R antagonists of Garnick et al. described in Table I. Also in col. 1, lines 11-63 of Garnick et al., a wide variety of prostate cancer treatments is described in addition to those described as the purported invention.

For suitable LHRH-R antagonists, see Garnick et al., col. 3, line 55 et seq. Table I alone lists 134 LHRH-R antagonists. As noted hereinabove, Garnick et al. does not teach, however, the use of any LHRH-R agonist in combination with calcitriol. Neither does Beer et al.

Neither Conway et al. nor Chen cure the foregoing defects of Garnick et al. and Beer et al.

Conway et al. is clearly inapposite, because it is directed to the treatment of neonatal hypocalcemia with an aqueous calcitriol solution. This has nothing to do with the presently claimed method for treating advanced prostate cancer.

Chen is also inapposite vis-a-vis the present claims. Chen teaches solubilizers for paclitaxel (col. 7, line 8) and possibly leuprolide (col. 7, line 23). These solubilizers are PEG-Vitamin Es, quaternary ammonium salts, PEG-monoacid fatty esters, PEG-glyceryl fatty esters, polysorbates PEG-fatty alcohols (col. 7, lines 13-18; col. 14, line 67 to col. 15, line3). Calcitriol clearly is not encompassed by the foregoing teaching, nor is calcitriol mentioned as an osteoporosis agent at col. 7, line 59, that can be solublilized using a paclitaxel solubilizer.

By no stretch of imagination does Chen teach a combination of leuprolide with calcitriol or a combination of leuprolide, calcitriol and polysorbate 20, much less the presently claimed method.

The general conditions of the claims have not been disclosed in the prior art for reasons advanced hereinabove. Accordingly, In re Aller, 220 F.2d 454, 456; 105 U.S.P.Q. 233, 235 (CCPA 1955) is inapposite.

The prior art compositions are clearly different, and are for a different purpose. Here again, as in the case of claims 1-4 and 16-23 discussed hereinabove, a *prima facie* case of obviousness to one of ordinary skill in the pertinent art has not been established. Withdrawal of the rejection based on obviousness is believed to be in order.

The references cited but not applied against the claims have been reviewed with interest. Those references do not vitiate the patentability of the present claims, however.

Early passing of this application to issue is solicited.

Respectfully submitted,

Dated: June 30, 2008

By _____
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CERTIFICATE OF FACSIMILE TRANSMISSION

I hereby certify that this AMENDMENT AND RESPONSE UNDER RULE 116 is being transmitted by facsimile transmission to Fax No. 571-273-8300 on June 30, 2008

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